

Mental Health Status and Quality of Life in Undiagnosed Glaucoma Patients

A Nationwide Population-Based Study

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Abstract: Glaucoma is a leading cause of irreversible vision loss. Mental health and quality of life (QoL) are important issues for patients with glaucoma because visual impairment can be related to those. Analysis of mental health status or QoL in undiagnosed glaucoma patients can be free of the bias caused by awareness of the disease itself. In this study, the association between mental health status or QoL and undiagnosed glaucoma, along with the effects of visual acuity or visual field damage was investigated. Among individuals in the Korea National Health and Nutrition Examination Survey (KNHANES) V (2010–2012), subjects 40 years or older were included. KNHANES is a cross-sectional study using a stratified, multistage, probability sampling survey. The KNHANES includes questionnaires to assess psychological health, including depression, sleep duration, psychological stress, and suicidal ideations. To evaluate QoL, the KNHANES includes the EuroQoL, which is composed of a health-status descriptive system (EuroQoL 5-dimension, EQ-5D) and the EQ visual analog scale (EQ-VAS). The proportion of people reporting symptoms of “some or severe problems” in all 5 dimensions of the EuroQoL-5 instrument, including anxiety/depression, was higher in the glaucoma group than in the nonglaucoma group. The subjective health status reported by the EQ-VAS was lower in the subjects with glaucoma than in those without glaucoma. Suicidal ideation was greater in subjects with glaucoma than in those without glaucoma ($P=0.005$). After adjustment for demographic factors, glaucoma subjects were more likely than those without glaucoma to have some or severe problems with anxiety/depression (odds ratio 1.77; 95% confidence interval, 1.26–2.49). Worse best corrected visual acuity was associated with more problems with a lower EQ-5D score in glaucoma subjects. Individuals who had undiagnosed glaucoma were more depressed than those without glaucoma. QoL can be affected by glaucoma, especially in patients with worse visual acuity.

Editor: Jacky Lee.

Received: January 3, 2016; revised: March 19, 2016; accepted: April 5, 2016.

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This study was supported by a grant from the Korean Health Technology R&D Project, Ministry of Health & Welfare, Republic of Korea (HI14C1731). The funding organization had no role in the design or conduct of this research.

The authors report no conflicts of interest.

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ISSN: 0025-7974

DOI: 10.1097/MD.0000000000003523

(*Medicine* 95(19):e3523)

Abbreviations: BCVA = best corrected visual acuity, CDR = cup-to-disc ratio, EQ-5D = EuroQoL 5-dimension, KNHANES = Korean National Health and Nutrition Exam Survey, QoL = quality of life, RNFL = retinal nerve fiber layer defect, SE = spherical equivalent, VA = visual acuity, VF = visual field.

INTRODUCTION

Mental health is an important area and influences health-related quality of life (QoL).¹ Depression, one of the most common mental diseases, is associated with worse QoL and increased mortality.^{2,3} Recently, depression has been found to be one of determinants for cardiovascular disease through alteration of the autonomic nervous system or inflammatory cytokines,⁴ which has been reported to have an association with glaucoma.^{5,6}

Patients with visual impairment have higher probability of being depressed than subjects without eye diseases.⁷ Visual disability can aggravate QoL through, for example, driving limitations and fear of falling, and it can be related to depression.^{8,9} Glaucoma is a common, chronic, progressive optic nerve disease that can cause irreversible visual impairment. A 10% to 20% prevalence of depressive symptoms has been reported in subjects with glaucoma.^{10–12} Despite the reported association between glaucoma and depression,⁷ no objective evaluation of vision, such as visual acuity (VA) or visual field (VF), has been related to depression severity.^{11,13,14} However, subjective measures of visual function have been linked to depression.^{11,13,14} The perception of disease itself could affect the sense of well-being in glaucoma patients through the fear of future vision loss, and the potential side effects of treatment might lead to mental health symptoms.^{11,13} Evaluating mental health status or QoL in undiagnosed glaucoma patients would remove the bias caused by acknowledgement of the disease itself, but no study has evaluated both psychological health and QoL in undiagnosed glaucoma patients.

The Korea National Health and Nutrition Examination Survey (KNHANES) is an ongoing, nationwide, population-based study that provides data on ophthalmologic examination, psychological health, and sociodemographic factors. Therefore, we used data from the KNHANES to investigate the association between mental health status and QoL in undiagnosed glaucoma, along with the effects of VA or VF damage.

METHODS

Study Population

This cross-sectional study was based on data from the KNHANES V (2010–2012), a nationwide epidemiological

survey conducted by the Division of Chronic Disease and Prevention, Ministry of Health and Welfare, with the approval of the institutional review board. The survey follows the tenets of the Declaration of Helsinki for biomedical research involving humans. Written informed consent was provided by all participants. The KNHANES uses a stratified, multistage, probability sampling method based on geographical area, age, and sex. This nationally representative study is composed of a Health Interview Survey, Health Examination Study, and a Nutrition Survey.

Among participants in the KNHANES 2010–2012 V, subjects 40 years or older who underwent ophthalmological examination were included. Participants who had previous retinal surgery, along with those whose fundus photograph displayed geographic atrophy or signs of wet age-related macular degeneration, such as retinal pigment epithelial (RPE) detachment, serous detachment of the sensory retina, subretinal or sub-RPE hemorrhage, or subretinal fibrous scars, were excluded. We excluded subjects with visually significant cataract (best corrected visual acuity [BCVA] of better eye worse than 0.5) and corneal opacity. Cataract was defined as lens opacities (LOCS III score is ≥ 2) including nuclear, cortical, posterior subcapsular, anterior capsular, or combined type compared with standard photographs, similar to previous studies.^{15–17} Individuals diagnosed with glaucoma by their doctor and those undergoing glaucoma treatment were also excluded.

Outcome Variables

The KNHANES includes questionnaires to assess psychological health, including depression, sleep duration, psychological stress, and suicidal ideations. To evaluate depression, subjects were asked, “Has your life been disrupted by feelings of hopelessness or sadness for more than two weeks within the past year?” Participants who responded “yes” to that question were classified as having depression. A diagnosis of depression indicates subjects diagnosed with a depressive disorder by a doctor. Psychological stress was graded from responses, which reflect cognitive complaints on a 4-point Likert scale: 1 (low), 2 (moderate), 3 (severe), and 4 (very severe). Self-reported sleep duration was divided into 5 categories: ≤ 5 , 6, 7, 8, and ≥ 9 hours/day. If participants replied “yes” to the question, “During the past year, have you ever had a suicidal ideation?” they were categorized as having suicidal ideations.

To evaluate QoL, the KNHANES includes the EuroQoL, which is composed of a health-status descriptive system (Euro-QoL 5-dimension, EQ-5D) and the EQ visual analog scale (EQ-VAS). The EQ-5D assesses the level of self-reported problems according to the 5 dimensions of mobility (EQ-1), self-care (EQ-2), usual activities (EQ-3), pain/discomfort (EQ-4), and anxiety/depression (EQ-5). Three answers for each dimension were possible (no problems, some problems, severe problems). The subjects who answered “some or severe problem” were defined as having a problem in the associated EQ 5-D dimension. Using a combination of the 5 dimensions, a summary index (EQ-5D index; range, -0.171 to 1) was calculated using the Korea valuation set developed by the Korean Centers for Disease Control and Prevention. The maximum score of 1 on the EQ5-D index represents the best health state with no self-reported problem in any of the 5 dimensions. Participants also expressed their subjective health status on a VAS ranging from 0 (the worst imaginable health state) to 100 (the best imaginable health state).

The KNHANES also collects data on anthropometrics and demographic characteristics, including socioeconomic status,

education level, and physical activity. Data on age, sex, educational level, and medical comorbidities such as diabetes mellitus and hypertension were also collected as potential confounding variables. Diabetes was defined as a fasting blood glucose level >126 mg/dL or current use of systemic antidiabetic treatment. Systemic hypertension was defined as a systolic blood pressure >160 mmHg, diastolic blood pressure >90 mmHg, or current use of systemic antihypertensive medication.

Participants were divided into nondrinkers, light-to-moderate drinkers (1 – 30 g alcohol/day), and heavy drinkers (>30.0 g alcohol/day). Smoking status was categorized into current smoker, nonsmoker, or ever-smoker. The physical activity scores were categorized based on the International PA Questionnaire guidelines. Moderate physical activity involved performance of moderate-intensity physical activity for >20 minutes 3 or 4 times/week, with moderate intensity exercise defined as that inducing a mild elevation in breathing or heart rate for at least 10 minutes.

Ophthalmological Evaluation

Participants underwent ophthalmological examinations, including fundus photography. Ophthalmologists measured intraocular pressure (IOP) using a Goldmann applanation tonometer (Haag-streit, Inc, Bern, Switzerland) and used a Topcon KR8800 autorefractor to obtain refractive error. Participant VA was measured at a distance of 4 m using an international standard vision chart (Jin vision chart based on the logMAR scale) based on decimal fractions.¹⁸ The BCVA was obtained with full subjective refraction using an autorefractometer, with the pinhole applied if the BCVA with autorefractometry did not improve to 0.8 . The BCVA was classified into 4 categories: 0.8 to 1.0 , 0.5 to 0.63 , 0.25 to 0.4 , and no light perception to 0.2 .

Participants with elevated IOP (≥ 22 mmHg) or a glaucomatous optic disc were examined using frequency-doubling technology (FDT, Humphrey Matrix; Carl Zeiss Meditec, Inc, Dublin, CA) with the N-30–1 program. A glaucomatous optic disc refers to any of the following: a horizontal or vertical cup-to-disc ratio (CDR) ≥ 0.5 , presence of optic disc hemorrhage, presence of a retinal nerve fiber layer (RNFL) defect, or a violation of the ISNT rule (neuroretinal rim thickness in the order of inferior $>$ superior $>$ nasal $>$ temporal).

A glaucoma diagnosis was made based on the ISGEO criteria¹⁹: category 1 requires a glaucomatous VF defect with a CDR ≥ 0.7 , asymmetry of a vertical CDR ≥ 0.2 , or presence of an RNFL defect.¹⁹ When the VF was unavailable or unsatisfactory, subjects were included in category 2 if their vertical CDR was ≥ 0.9 , vertical CDR asymmetry was ≥ 0.3 , or if they had an RNFL defect with violation of the ISNT rule.^{19,20} If examination of the optic disc and a VF test were not possible, category 3 required a VA $< 3/60$ and IOP exceeding 21 mmHg.^{19,20} VF score was measured as follows: One point for VF defects of $P < 0.01$, 3 points for $P < 0.005$, and 5 points for VF defects indicated as “not seen at maximum” in 18 locations of 1 eye. Abnormality score of VF was calculated providing greater weight on the location in the paracentral VF, as Brusini et al suggested.²¹ The sum of points in both eyes was used to determine glaucoma stage (mild versus advanced) based on the median value of the summed points.

Statistical Analyses

SAS software (ver. 9.2; SAS Institute, Inc.) was used for statistical analyses in order to reflect sampling weights and offer

nationally representative prevalence estimates. Demographic factors between subjects with and without glaucoma were compared using Student *t* test for continuous parameters and the χ^2 test for categorical variables. Continuous and categorical parameters are described as mean \pm standard error and percentage, respectively. Multivariate adjusted logistic analysis was performed to investigate factors associated with glaucoma. Factors that showed a difference between the 2 groups with $P < 0.05$ were entered into a multivariate analysis, and odds ratios (ORs) and 95% confidence intervals (CIs) were calculated. A P value < 0.05 was considered to indicate statistical significance.

RESULTS

Among the 25,534 participants in the KNHANES 2010–2012 V, 12,976 subjects 40 years or older were included in the present study (Figure 1). Among them, 12,881 individuals who underwent ophthalmological examination were selected. Of these, 155 participants who had previous retinal surgery, 89 subjects with a fundus photograph showing signs of wet age-related macular degeneration or geographic atrophy, and 18 individuals diagnosed with glaucoma or undergoing glaucoma treatment were excluded. In addition, 326 subjects were excluded because of incomplete medical data. After that, 214 subjects with visually significant cataract and corneal opacity were excluded. Ultimately, 12,079 participants (5235 males, 6844 females) were included in this study.

The prevalence of undiagnosed glaucoma was 4.27% \pm 0.25% in the study population. The mean age \pm standard error of subjects with glaucoma was 61.47 \pm 0.70 years (Table 1). Participants with glaucoma were older and less educated, less likely to live with a spouse, and exercised less regularly than those without glaucoma. According to univariate analysis, male sex, lower body mass index, presence of chronic disease such as diabetes or hypertension, and lower income status were related to glaucoma. BCVA was lower in subjects with glaucoma than in those without glaucoma.

Table 2 shows the univariate associations between glaucoma and psychological health and QoL parameters. Glaucoma is related to short (≤ 5 h) or long (≥ 9 h) sleep duration ($P = 0.041$). Suicidal ideation was greater in subjects with glaucoma than in those without glaucoma ($P = 0.005$). Depression diagnosed by a doctor did not differ significantly between

individuals with and without glaucoma. However, glaucoma was associated with depressive mood (≥ 2 weeks in a row) ($P = 0.037$). The proportion of anxiety/depression symptoms reported on the EQ-5 was higher in subjects with glaucoma than in those without glaucoma ($P < 0.001$). The glaucoma group also presented a higher proportion of those who reported “some or severe problems” in all 5 dimensions of the EQ-5 in comparison with the non-glaucoma group. The EQ-5D index and the subjective health status reported by the EQ-VAS were lower in the subjects with glaucoma than in those without glaucoma.

Table 3 presents the differences in psychological health and QoL between the subjects with and without glaucoma after adjusting for age (Model 1) and age, sex, body mass index, diabetes, hypertension, income status, education level, marital status, and regular exercise (Model 2: demographic factors with P value < 0.05 in univariate analyses). In both Models 1 and 2, glaucoma subjects were more likely than those without glaucoma to have some or severe problems with anxiety/depression (Model 1: OR, 1.71; 95% CI 1.23–2.39, Model 2: OR 1.77; 95% CI, 1.26–2.49). The multivariate OR for the lowest quartile of EQ-VAS in the glaucoma group versus the nonglaucoma group was 1.55 (95% CI 1.21–1.98) in Model 1 and 1.52 (95% CI 1.19–1.96) in Model 2.

Table 4 shows the results of subgroup analysis in individuals with glaucoma with regard to psychological health and QoL according to BCVA. As BCVA decreased, the EQ-5D index score also decreased ($P = 0.021$). Subjects with lower BCVA were more likely to have some or severe problems with anxiety/depression in the subgroup with glaucoma, but the relationship between them was not statistically significant ($P = 0.154$). The median value of the VF scores was 0. Subjects with points ≤ 0 and those with > 0 did not differ significantly in EQ-VAS or EQ-5D ($P = 0.357, 0.802$, respectively). EQ-5 (anxiety/depression) was not significantly correlated with abnormality score of VF defects ($P = 0.784$).

DISCUSSION

We present the first report regarding both psychological health and QoL in people with undiagnosed glaucoma. Subjects with glaucoma showed greater odds of having some or severe problems with anxiety/depression. In addition, glaucoma can lower QoL in patients even when they are unaware they have the disease.

One previous hospital-based study showed that the prevalence of depressive symptoms did not differ according to the presence of glaucoma.²² However, a growing body of evidence, including a population-based study, suggests that glaucoma patients are more likely to be depressed than subjects without glaucoma.^{10–12} The US National Health and Nutrition Examination Survey reported that glaucoma is significantly associated with depression after adjusting for demographic factors.¹¹ No large, cross-sectional studies have investigated the association between glaucoma and depression in Asian countries.

In this study, we discovered no significant difference between subjects with and without glaucoma in depression diagnosed by a doctor. However, glaucoma subjects were more likely to have self-reported depressive mood for ≥ 2 weeks ($P = 0.037$). A higher proportion of subjects with glaucoma (20.4%) than without glaucoma (11.7%, $P < 0.001$) reported symptoms of some or severe anxiety/depression on the EQ-5. In multivariate analysis, only EQ-5D (anxiety/depression) remained a significant correlation with glaucoma. Therefore,

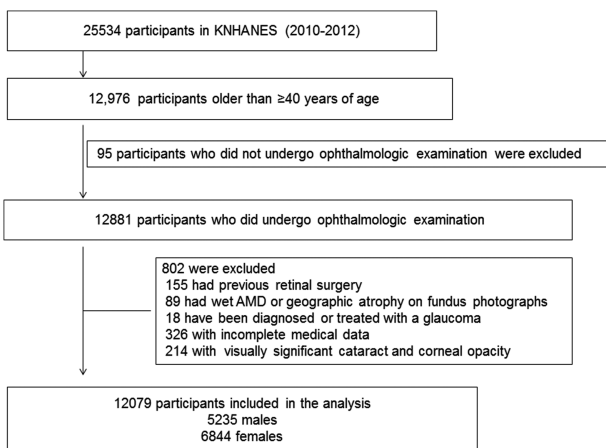


FIGURE 1. Flow diagram showing selection of study participants. AMD = age-related macular degeneration.

TABLE 1. Baseline Characteristics

	No Glaucoma (n = 11,509)	Glaucoma (n = 570)	P
	N = 20,870,020	N = 930,084	
Age, y	55.18 ± 0.17	61.47 ± 0.70	<0.001
Sex (% of female)	6,561 (52.2)	283 (42.4)	<0.001
Body mass index, kg/m ²	24.09 ± 0.04	23.60 ± 0.18	0.007
Waist circumference, cm	82.84 ± 0.14	82.63 ± 0.53	0.705
Diabetes	1561 (12.2)	105 (16.6)	0.015
Hypertension	4824 (38.0)	313 (53.3)	<0.001
Income status (high)	5743 (53.0)	202 (39.7)	<0.001
Education level (high)	5591 (54.9)	186 (38.5)	<0.001
Current smoker, %	2030 (22.3)	105 (24.9)	0.299
Heavy drinker, %	1000 (17.2)	38 (15.1)	0.494
Marital status (marriage, %)	9466 (82.8)	419 (75.2)	<0.001
Regular exercise (≥mod intensity, %)	5147 (44.3)	219 (36.8)	0.005
Daily sun exposure			0.066
<2 h	6983 (60.3)	324 (56.6)	
2–5 h	2652 (24.0)	127 (22.7)	
≥5 h	1851 (15.7)	117 (20.7)	
Best corrected visual acuity			<0.001
0.8–1.0	10,695 (94.8)	476 (86.3)	
0.5–0.63	775 (4.9)	85 (12.0)	
0.25–0.4	30 (0.3)	5 (1.1)	
No light perception to 0.2	9 (0.1)	4 (0.6)	

Statistically significant values ($P < 0.05$) are shown in bold.

depressive mood was more common in subjects with glaucoma, but the degree or duration of depressive symptoms was not severe enough to diagnose a major depressive disorder. When previous studies analyzed the relationships between glaucoma and depressive symptoms, they used different criteria for depressive mood. Wang et al found that the prevalence of

depression diagnosed by the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) was 10.9% in glaucoma patients and 6.9% in subjects without glaucoma ($P = 0.02$). They used self-reported glaucoma to investigate the relationship between glaucoma and depression, which could explain the discrepancy with the results of our study. In our study, subjects with

TABLE 2. Association Between Glaucoma and Psychological Health, Health-Related Quality of Life

	No Glaucoma	Glaucoma	P
Sleep duration, h			0.041
≤5	2414 (19.6)	149 (23.9)	
6	2998 (26.7)	137 (25.6)	
7	3054 (27.1)	126 (20.8)	
8	2298 (20.2)	109 (22.0)	
≥9	745 (6.4)	49 (7.7)	
Psychological stress (≥severe, %)	2627 (24.2)	125 (21.9)	0.360
Depressed mood (≥2 weeks in a row, %)	1566 (13.9)	97 (18.3)	0.037
Depression diagnosis (yes, %)	537 (28.4)	27 (26.5)	0.750
Suicide thoughts (yes, %)	1673 (14.7)	108 (20.1)	0.005
Psychological counseling (yes, %)	250 (2.3)	11 (1.7)	0.481
Quality of life			
EQ-1 (some or severe): physical activity	2342 (17.8)	177 (29.0)	<0.001
EQ-2 (some or severe): self-control	674 (4.9)	58 (10.1)	<0.001
EQ-3 (some or severe): daily activity	1446 (10.8)	107 (18.7)	<0.001
EQ-4 (some or severe): pain	3094 (24.8)	182 (31.1)	0.013
EQ-5 (some or severe): anxiety/depression	1413 (11.7)	100 (20.4)	<0.001
EQ_VAS	73.15 ± 0.23	67.18 ± 1.25	<0.001
EQ_5D	0.93 ± 0.00	0.89 ± 0.01	<0.001

EQ-VAS = EQ visual analog scale. Statistically significant values ($P < 0.05$) are shown in bold.

TABLE 3. Adjusted Odds on Multivariate Analysis of the Association Between Glaucoma and Psychological Health, Health-Related Quality of Life

	No Glaucoma	Glaucoma Odds Ratio (95% CI)
Model 1		
Sleep duration (≤ 5 hr)	1	1.04 (0.79–1.37)
Depressed mood (≥ 2 weeks in a row)	1	1.31 (0.97–1.78)
Suicide thought (yes)	1	1.21 (0.92–1.60)
EQ_VAS (lowest quartile, %)	1	1.55 (1.21–1.98)
EQ_5D (lowest quartile, %)	1	1.26 (0.97–1.63)
EQ_5D	1	
EQ_1 (some or severe): physical activity	1	1.23 (0.93–1.62)
EQ_2 (some or severe): self-control	1	1.40 (0.93–2.12)
EQ_3 (some or severe): daily activity	1	1.26 (0.90–1.75)
EQ_4 (some or severe): pain	1	1.08 (0.83–1.41)
EQ_5 (some or severe): anxiety/depression	1	1.71 (1.23–2.39)
Model 2		
Sleep duration (< 5 hr)	1	1.00 (0.76–1.33)
Depressed mood (≥ 2 weeks in a row)	1	1.32 (0.97–1.79)
Suicide thought (yes)	1	1.21 (0.92–1.59)
EQ_VAS (lowest quartile, %)	1	1.52 (1.19–1.96)
EQ_5D (lowest quartile, %)	1	1.32 (1.00–1.74)
EQ_5D	1	
EQ_1 (some or severe): physical activity	1	1.28 (0.96–1.71)
EQ_2 (some or severe): self-control	1	1.38 (0.91–2.11)
EQ_3 (some or severe): daily activity	1	1.23 (0.87–1.73)
EQ_4 (some or severe): pain	1	1.16 (0.88–1.54)
EQ_5 (some or severe): anxiety/depression	1	1.77 (1.26–2.49)

Model 1; age adjustment; Model 2; age, sex, BMI, diabetes, hypertension, income status, education level, marital status, and regular exercise adjustment. CI = confidence interval, EQ-VAS = EQ visual analog scale.

Statistically significant values ($P < 0.05$) are shown in bold.

glaucoma undiagnosed by a doctor may have been free of the perception of the disease and the fear of the potential side effects of treatment. Therefore, they might have experienced depressive symptoms that were not serious enough to warrant a depression diagnosis.

The depressive symptoms were simply categorized for the subjects who answered “some or severe problem” for anxiety/depression (EQ-5) in this study. Self-report instruments for common mental disorders include the Patient Health

Questionnaire, the Center for Epidemiological Studies Depression (CES-D) scale, Beck Depression Inventory, and State-Trait Anxiety Inventory.^{11,13,23} Detailed grading for anxiety/depression such as “State-Trait Anxiety Inventory” could not be performed in this study.^{24,25} In addition, it was not clear whether anxiety/depression is a temporary condition to symptom or a general tendency in subjects with undiagnosed glaucoma. It could be one of limitations that quantitative or qualitative evaluation for depression was not possible in this study, even

TABLE 4. Relationship of Visual Acuity and Visual Field Damage and Health-Related Quality of Life in Subjects With Undiagnosed Glaucoma

	EQ-VAS	EQ-5D	EQ_5 (Severe or Some): Anxiety/Depression
Best corrected visual acuity			
0.8–1.0	67.92 ± 1.38	0.90 ± 0.01	80 (19.1)
No light perception –0.63	62.10 ± 3.39	0.82 ± 0.03	20 (29.1)
P^*	0.118	0.021	0.154
Visual field score			
Mild (58.2%)	68.17 ± 1.70	0.89 ± 0.01	53 (21.0)
Severe (41.8%)	65.83 ± 1.87	0.89 ± 0.01	47 (19.5)
P^*	0.357	0.802	0.784

EQ-VAS = EQ visual analog scale.

*Statistically significant values ($P < 0.05$) are shown in bold.

though a brief screening questionnaire needed a shorter time. In addition, the information on mental health and QoL came from self-reported questionnaires, so reporting bias is possible.

For glaucoma patients, fear of blindness and the potential adverse effects of treatment can lead to depression.²⁶ Previous reports on the association of glaucoma with mental health status have concentrated on glaucoma patients with preexisting disease. Jampel et al¹³ found that depressive mood was related to patient perceptions of worsening visual function but not to poor VA or worse VF in newly diagnosed glaucoma patients. That study eliminated the effects of treatment itself because patients were not informed about their treatment at the time of the QoL interview; however, it could not adjust for the effects of perception of disease.¹³ Our study, which excludes the effects of fear about the illness, corresponded to their study: the VA and VF scores did not correlate with depressive symptoms. Even without knowing about the disease itself, subjectively perceived poorer vision seems to be more closely related to depressive mood than the objective evaluation of vision.

Glaucoma influences QoL in a degree similar to other chronic diseases such as dementia and diabetes.²⁷ Patients with glaucoma in a cross-sectional study acknowledged that their QoL was decreased compared with subjects without glaucoma.²⁸ In our study, subjects with glaucoma reported more problems with anxiety/depression on the EQ-5D. To evaluate QoL in glaucoma patients, general health-related, vision-specific, and glaucoma-specific instruments can be used. As general health-related questionnaires, EQ-5D or Short-Form Health Surveys (SF-36) have been widely used: as vision-specific measurements, National Eye Institute Visual Functioning Questionnaire (NEI-VFQ) or Activities of Daily Vision Scale (ADVS), Visual function index (VF-14); as glaucoma-specific instruments, Glaucoma Quality of Life (GQL)-15, or Symptom Impact Glaucoma (SIG).^{27,29} Disease-specific instruments can focus on the issues of particular concern such as vision with more responsiveness (sensitive to change).³⁰ General QoL instruments lack the responsiveness of the disease-specific instruments and the information focused on visual function.²⁷ Among glaucoma-specific instruments, GQL-15 revealed that the most problematic activities for glaucoma patients were those associated with dark adaptation.^{29,31} Those ocular dependent factors were not evaluated in general QoL instruments such as the Euro QoL. That the Euro QoL does not assess vision-specific function was one of limitations of this study. However, valid and generic questionnaires may work even better with multidimensional evaluation of QoL.^{27,32} Combination of generic and disease-specific instruments may be a good approach to evaluate health-related QoL in further studies.³²

Decreasing BCVA was associated with low EQ-5D score in glaucoma subjects. Those results correspond with a previous hospital-based study that found that the EQ-5D index was correlated with VA in glaucoma patients.³³ However, VF score was not related to EQ-5D index. Several studies reported that the severity of VF defects was linked to impaired QoL or opposite results.^{29,34–36} The different study findings may result from dissimilar strategy used for grading QoL or the proportion of individuals with advanced glaucoma, or the type of VF tests. In our study, FDT was used to evaluate VF damage, whereas other reports employed standard automated perimetry.^{31,37,38} Using standard automated perimetry, visual field index was correlated with GQL-15, one of QoL assessment tools, not corresponding to our findings.³¹ The visual field index is primarily based on the pattern deviation maps in eyes with a

mean deviation better than -20 dB with weighting toward the central areas of the VF, leading to be less affected by media opacities.³⁹ N-30-1 program with a scoring algorithm in frequency doubling technology is not ideal for evaluating glaucoma stage and may be one of limitations of our study, even though that grading system has been found to be highly specific for glaucoma detection.^{21,40}

A growing body of evidence shows that depression increases the risk of coronary artery disease to at least 1.5 times that of healthy subjects.² Depression is associated with autonomic dysfunction with increased sympathetic tone and endothelial dysfunction and inflammation.² Some of those symptoms have also been reportedly associated with glaucoma.^{5,6,41,42} Therefore, common risk factors could lead to correlation between glaucoma and depression. The relationship between undiagnosed glaucoma and depressive symptoms may also suggest a possibility that depression may increase the risk of glaucoma development. However, we cannot confirm a cause and effect relationship from the present study because our cross-sectional study revealed only the association between glaucoma and depression.

The strength of this study is that a population-based study is representative of individuals with undiagnosed glaucoma in the general population. The KNHANES includes information on socioeconomic status and demographic factors that contribute to psychological health, such as income status, education level, marital status, and daily sun exposure. Therefore, we could adjust all those factors to assess the association between glaucoma and mental health.

In conclusion, individuals who had undiagnosed glaucoma might be more depressed than those without glaucoma, even though the degree of depression is not sufficient to diagnose depression. QoL can be affected by glaucoma, especially in patients with worse visual acuity. Therefore, when initially diagnosing glaucoma, acknowledging that glaucoma patients might already have depressive symptoms could be helpful in treatment and follow-up.

ACKNOWLEDGMENTS

The authors thank Professor Ki Ho Park, Department of Ophthalmology, Seoul National University College of Medicine and Professor Chan Yun Kim, Department of Ophthalmology, Institute of Vision Research, Yonsei University College of Medicine for reviewing this article. We report this result on behalf of the Epidemiologic Survey Committee of the Korean Ophthalmological Society.

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